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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,472	12/14/2001	Christopher Kern	02481.1767	1068

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Finnegan, Henderson, Farabow,
Garrett & Dunner, L.L.P.
1300 I Street, N.W.
Washington, DC 20005-3315

EXAMINER

LEWIS, PATRICK T

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/014,472

Applicant(s)

KERN ET AL.

Examiner

Patrick T. Lewis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-8 and 26-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-8 and 26-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 26, 2005 has been entered.

Election/Restrictions

2. Applicant's election with traverse of Group I in the reply filed on December 19, 2002 is acknowledged. The requirement was made FINAL in the Office Action dated March 26, 2003.

Applicant's Response Dated January 26, 2005

3. Claims 1, 3-8 and 26-30 are pending. An action on the merits of claims 1, 3-8 and 26-30 is contained herein below.

4. The rejection of claims 1, 4 and 6-8 under 35 U.S.C. 102(b) as being anticipated by Yeda Research and Development WO 92/19249 (Yeda) is maintained for the reasons of record as set forth in the Office Action dated August 24, 2004.

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5. Applicant's arguments with respect to claims 3 and 5 under 35 U.S.C. 102(b) as being anticipated by Yeda Research and Development WO 92/19249 (Yeda) have been considered but are moot in view of the new ground(s) of rejection.

6. The rejection of claims 19-26 under 35 U.S.C. 112, first paragraph, has been rendered moot in view of applicant's response dated January 26, 2005 (November 3, 2004).

Rejections of Record Set Forth in the Office Action Dated August 24, 2004

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 1, 4 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeda Research and Development WO 92/19249 (Yeda).

9. Applicant's arguments filed January 26, 2005 have been fully considered but they are not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the treatment of osteoarthroses or disorder that is not linked to pathological process involving induction of TNF- α secretion) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 3, 5 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeda Research and Development WO 92/19249 (Yeda) and Claiborne et al. US 6,291,457 (Claiborne) in combination.

Claims 3, 5 and 26-30 are drawn to a method of treating a disorder comprising administering to a subject a therapeutically effective amount of enoxaparin, wherein the disorder is one or more of a wound healing disturbance, a disorder of the locomotor system, and a disturbance of bone metabolism. Claim 3 further limits the disorder. Claims 5, 26-27 and 30 limit the modes of administration. Claims 28-29 limit the dosage regimen.

Yeda teaches the treatment of pathological processes involving the induction of TNF- α secretion using a pharmaceutically acceptable carrier and a low molecular

weight heparin (LMWH) (Abstract). The LMWH is present in a low effective dose and is administered at intervals of about 5-8 days. The LMWH is capable of inhibiting *in vitro* TNF- α secretion by resting T cells and/or macrophages in response to T cell-specific antigens, mitogens, macrophages activators, disrupted extracellular matrix (dECM), laminin, fibronectin, and the like. TNF- α is involved in the pathogenesis of many undesirable inflammatory conditions in autoimmune diseases, graft rejection, vasculitis and atherosclerosis (page 3, lines 18-25). For these reasons, ways have been sought to regulate the secretion of TNF- α as a means to control a variety of diseases. The pharmaceutical composition may be administered in any manner as dictated by the particular application at hand including, but not limited to, enteral administration (including oral) or parenteral administration (including topical or inhalation with the aid of aerosols) (page 7, line 34 to page 8, line 24). The compositions typically contain a single low dose unit of less than 5 mg LMWH, preferably from about 0.3 to about 3 mg, and most preferably contain from 1 to 1.5 mg. LMWHs to be used in the method include enoxaparin which is commercially available (page 10, line 15 to page 11, line 34).

Yeda differs from the instantly claimed invention in that Yeda does not explicitly teach the treatment of osteoarthroses, spondyloses, chondrolysis, collagenoses, arthropaties, and myalgias. Yeda also does not explicitly teach intraarticular injections of enoxaparin; however, these deficiencies would have been obvious to one of ordinary skill in the art at the time the invention was made.

Claiborne teaches that excessive or unregulated TNF production or activity has been implicated in mediating or exacerbating rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, and other arthritic conditions, sepsis, septic shock, endotoxic shock, gram negative sepsis, toxic shock syndrome, adult respiratory distress syndrome, cerebral malaria, chronic pulmonary inflammation disease, silicosis, pulmonary sarcosis, bone resorption diseases, reperfusion injury, graft v. host rejection, allograft rejections, fever and myalgia due to infection, cachexia secondary to infection or malignancy, cachexia secondary to AIDS, AIDS related complex (ARC), keloid formation, scar tissue formation, Crohn's disease, ulcerative colitis and pyresis (column 1, lines 40-53).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat one or more of osteoarthroses, spondyloses, chondrolysis, collagenoses, arthropaties, and myalgias by administering to a subject a therapeutically effective amount of enoxaparin. Yeda teaches the treatment of pathological processes involving the induction of TNF- α secretion using enoxaparin within the dosage range instantly claimed. Although Yeda does not explicitly teach the treatment of osteoarthroses, spondyloses, chondrolysis, collagenoses, arthropaties or myalgias, it would have been obvious to one of ordinary skill in the art at the time of the invention to do so since Claiborne teaches that excessive or unregulated TNF production or activity has been implicated in mediating or exacerbating a variety of conditions including rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, and other arthritic conditions, reperfusion injury, graft v. host rejection, allograft rejections, fever

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and myalgia due to infection, keloid formation, scar tissue formation, Crohn's disease, ulcerative colitis and pyresis. One of ordinary skill in the art would have been motivated to do so in view of the links between the induction of TNF- α secretion and the instantly claimed pathological processes. The selection of an appropriate mode of administration (i.e. intraarticular injection) would have been well within the purview of one of ordinary skill in the art at the time of the invention. As suggested by Yeda, the mode of administration would be dictated by the particular application at hand.

Conclusion

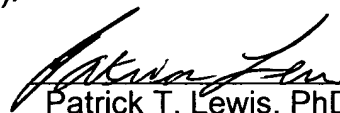
13. Claims 1, 3-8 and 26-30 are pending. Claims 1, 3-8 and 26-30 are rejected. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Patrick T. Lewis, PhD
Examiner
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